Prognostic significance of DNMT3A mutations in patients with acute myeloid leukemia

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Acute myeloid leukemia (AML) represents a heterogeneous group of malignancies with great variability in clinical course and response to therapy. Several molecular markers have been described that help to classify AML patients into risk groups. Mutations in DNA methyltransferase 3A (DNMT3A) gene were recently demonstrated in AML. Approximately 20% patients with AML carry DNMT3A gene mutations and were associated with a poor clinical outcome but its clinical implications in Egyptian AML patients are largely unknown.

The aim of the study: was to study the incidence and prognostic impact of DNMT3A mutations in patients with de novo acute myeloid leukemia.

Subjects and methods: A total of 120 patients with de novo AML were examined for mutations in DNMT3A by sequencing.

Results: DNMT3A mutations were identified in 34/120 (28%) of AML patients. 15 patients with M4, 14 patients with M5, 3 patient with M2 and 2 patient with M6. DNMT3A mutations were more frequently associated with older age, higher platelet counts and intermediate risk. DNMT3A-mutated patients did not differ regarding complete remission (CR) and disease-free survival (DFS), but had shorter overall survival (OS; P= 0.048) than DNMT3A-wild-type patients. Mutations in DNMT3A independently predicted a shorter OS (P = 0.049) by multivariate analysis.

Conclusion: We concluded that DNMT3A mutations are highly frequent in Egyptian patients with AML and are associated with an unfavorable prognosis.

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